



HAEMANGIOMAS AND VASCULAR MALFORMATIONS

ORAL ITRACONAZOLE FOR TREATMENT OF INFANTILE HEMANGIOMAS: UPDATED CLINICAL AND MECHANISM RESEARCH

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Introduction: Infantile hemangiomas (IHs) can present a therapeutic challenge to clinicians, especially when associated with severe pain and feeding difficulties. The standard therapeutic management includes corticosteroids and propranol. However, the clinical response is not always satisfactory.

Objective: We report a case series of IHs which were successfully treated with oral itraconazole (ITR), and, the possible action mechanism updated.

Materials and Methods: The diagnosis and judgment the improvement of IHs based on clinical manifestations, noninvasive color Doppler ultrasound performance, dermoscopy, and, magnetic resonance imaging observation. Informed consent was signed from IHs baby's parents after enough communication. In vitro, the expression of sonic hedgehog (Shh), the proliferation, cell cycle analysis by flow cytometry, apoptosis, angiogenesis, migration, and tube formation of hemangioma endothelial cells (HemECs), response to ITR were investigated.

Results: Totally 38 IHs babies (male/female=10/28) entered the treatment, they aged 1-10 (mean 3.5) months, weight 4-11 kg. Five cases associated with fungal infection (3 *Candida* spp., and 2 *Malassezia* spp.). ITR capsules (15 cases) or oral solution (23 cases) with dosage of 5 mg/kg/d was applied. In the first month, the red color of the lesions became lighter and the growth of the lesions were controlled, small cracks and wrinkles appeared on the surface which divided the lesion into lobules, dermoscopic feature showed indistinct vascular network and less capillary branches. The treatment period ranged 9-275 (mean 87.4) days, with the dosage of 280-9000 (mean 2946) mg. The clinical effective percentage was 71.05% (27/38). Compliance was judged to be very good with 1/3 mild, reversible diarrhea that did not interrupt medication.

Conclusions: Investigation in vitro of ITR to IHs indicated that induces of hemangioma endothelial cells mitochondrial swelling, affects cell energy metabolism, down regulation of Hedgehog and PI3K-AKT-mTOR signaling pathways, autophagy and apoptosis are possible mechanisms of ITR works.

